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THE CAUSE OF DEATH IN STRANGULATION OBSTRUCTION: AN EXPERIMENTAL STUDY

I. CLINICAL COURSE, CHEMICAL, BACTERIOLOGIC AND SPECTROPHOTOMETRIC STUDIES*

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THE MORTALITY IN ACUTE intestinal obstruction has decreased from around 60 per cent at the turn of the century to 10 to 20 per cent in the larger clinics at the present time (Table I). A comparison of different series of cases from the same clinic over the period of years further demonstrates this decline—University of Pennsylvania;[7, 9, 19] Massachusetts General Hospital;[3, 4, 10, 16] Johns Hopkins Hospital;[5, 20] University of Minnesota Hospitals.[14, 18]

This decline in mortality, however, has been manifested more in cases of simple obstruction than in strangulation obstruction.[6, 16, 19] In 1947, Eliason and Welty[19] reported a mortality of only one per cent in those cases of obstruction not complicated by strangulation or carcinoma. On the other hand, even as late as 1940, Schlicke, Bargen and Dixon[17] reported a mortality of 56 per cent of those cases where gangrenous bowel was found at operation, and even more recent reports showed a mortality of 20 to 40 per cent in this group of patients.[18-20] It is of particular interest to note that although at the present time interference with the circulation occurs in only 17 to 33 per cent of the total cases,[16-20] the mortality ranges between 25 and 40 per cent, and these cases account for more than half of the total deaths reported in the various series.[16-18, 20] The continued high mortality in cases of strangulation obstruction indicates that factors other than those amenable to present improved methods of management exist in this condition.

We have investigated the problem of strangulation obstruction utilizing certain of the newer concepts of management in an attempt to further clarify the cause of death. Following the creation of a strangulated ileal obstruction in dogs, the animals were treated for hemorrhage, shock, dehydration and electrolyte loss, and studies were made on the blood, peritoneal fluid, and gut contents.

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METHODS

Seven carefully selected, vaccinated, dewormed adult mongrel dogs weighing between 9.4 and 17.0 Kg. were used in this experiment. Following a 24 hour period of starvation, the animals were operated upon under Na pentobarbital (24.0 mg. per Kg.) anesthesia. Samples of blood for control chemical studies were taken on the day before or the morning of operation. Strict aseptic technic was used throughout. All the omentum distal to the spleen was excised in order to facilitate the withdrawal of peritoneal fluid and to obviate the omentum as a source of revascularization of the strangulated segment.[22] At a point between 100 and 150 cm. from the ligament of Trietz, the bowel was severed and the cut ends closed by the Parker-Kerr technic (Fig. 1). Fifteen centimeters above the proximal closed end a 30 cm. segment of bowel was strangulated by doubly ligating the veins in the base of the mesentery. The communicating arteries and veins at either end of the

TABLE I

Year Reported	Period Covered	Author	Hospital	No. of Cases	Mortality
					%
1888	1880–1883	Fitz[1]	Collected	146	70.0
1900	Up to 1900	Gibson[2]	Collected	1000	43.0
1908	1898–1907	Scudder[3]	Mass. General	121	60.0
1920	1908–1917	Richardson[4]	Mass. General	118	50.0
1921	1912–1921	Finney[5]	Johns Hopkins	245	36.0
1925	1900–1925	Van Buren and Smith[6]	Collected	1089	41.8
....	1914–1923	.....	Presbyterian	174	58.0
1929	1905–1922	North[7]	Univ. of Pa.	200	30.5
1925	Up to 1925	Souttar[8]	Collected	3064	32.0
1929	1922–1928	Brill[9]	Univ. of Pa.	124	36.3
1932	1918–1927	McIver[10]	Mass. General	335	31.0
1929	1924–1929	Miller[11]	Charity Touro Infir.	343	61.0
1934	1922–1932	Christopher and Jennings[12]	Evanston	127	44.9
1938	Up to 1938	Scudder[13]	Collected	2150	24.0
1938	1931–1938	Wangensteen[14]	Univ. of Minn.	156	17.9
1940	1936–1939	Johnston[15]	Wayne Univ.	63	19.1
1940	1927–1938	McKittrick and Sarris[16]	Mass. General	136	20.0
1940	1938–1939	Schlicke, Bargen and Dixon[17]	Mayo Clinic	166	22.0
1943	1938–1942	Dennis and Brown[18]	Univ. of Minn.	110	15.5
1947	1934–1943	Eliason and Welty[19]	Univ. of Pa.	292	11.0
1946	1936–1945	Calihan, Kennedy and Blain[20]	Johns Hopkins	204	20.0
1946	1943–1945	Moses[21]	Gallinger Municipal	118	8.0

strangulated segment, running parallel and adjacent to the bowel on the mesenteric border, were severed and doubly ligated. A segment of plastic tubing was threaded through normal bowel into the strangulated segment; two multiperforated latex tubes were placed in the lateral gutters; all tubes were brought out onto the anterior abdominal wall through stab wounds, and the abdomen was closed. At the conclusion of the procedure the strangulated segment was invariably dusky blue in color, and in some cases had begun already to exude a pink serous transudate.

Another segment of plastic tubing was then threaded through the jugular vein into the superior vena cava, anchored to the skin, and then connected to a gravity drip, thus enabling the animal to receive large amounts of fluids constantly while moving freely about in his cage.

Parenteral fluid administration was begun at operation and continued con-

stantly throughout the period of survival, the amount and type of fluid, *i.e.*, blood, glucose and saline or gelatin, being determined by the hematocrit and hemoglobin at two or four hour intervals and by the clinical condition of the animal. Postoperatively, usually at four hour intervals, the peritoneal cavity and gut were aspirated, and blood samples were withdrawn from the femoral artery for serial studies. In all instances all the peritoneal fluid obtainable from the latex tubes at each interval was removed under sterile conditions. In six of the seven animals, only several cubic centimeters of bowel contents were removed for chemical determinations. In the remaining animal (No. 347), the gut contents were evacuated as completely as possible at four hour intervals. Blood and peritoneal fluid cultures were taken at various intervals, and gut contents were cultured just prior to death in a number of the animals.

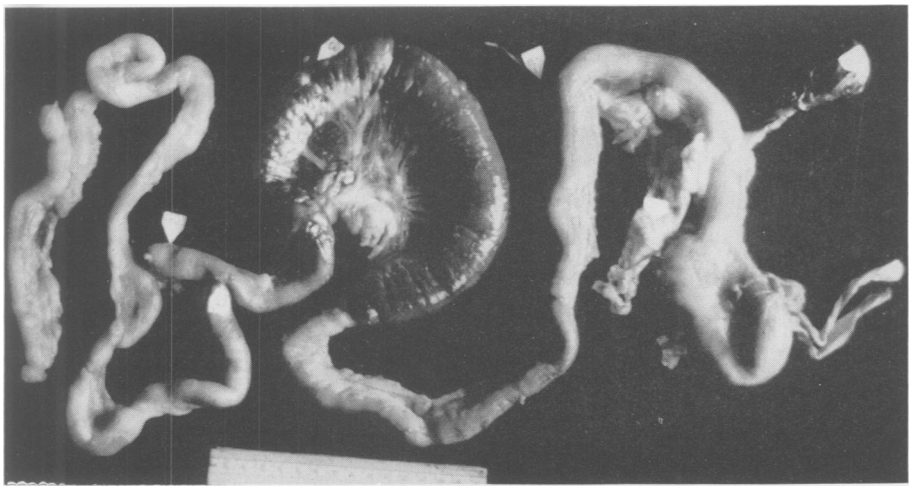


FIG. 1.—Photograph of strangulated segment of bowel from dog No. 331. The distal turned in end was sutured to the side of the proximal closed end in order to prevent intussusception. This was the usual picture noted in five of the seven dogs (see text).

The following chemical determinations were done: specific gravities;[23] proteins;[24] urea nitrogen;[25] nonprotein nitrogen;[26] creatinine;[26] uric acid;[27, 28] total nitrogen;[29] amino acid nitrogen;[30] amylase;[31] lipase;[32] chlorides;[33] calcium;[34] CO_2 combining power;[35] pH;[36] potassium[37] and spectrophotometric studies.[38]*

* The absorption spectrum curves are plots of *fractional molecular extinction coefficients,* ϵ (at concentration, $C=$ 1 mM per liter, and at depth, $d=$ 1 cm.), against wave-length in mu, ϵ is a negative logarithmic function of the amount of light transmitted by the solution, much the same as pH is the negative log. of H^+, the hydrogen ion concentration, ϵ, not the light transmitted, is proportional to the concentration. Molar concentrations of reference for hemin derivatives refer to the weight containing one iron atom; in the case of hemoglobin the equivalent weight is 16,700, and 1 mM. per liter equals 16.7 Gm. per liter, or 1.67 Gm. per 100 ml. The millimolar concentration has proved convenient and unequivocal for the spectrophotometric notation of the various hemin derivatives.[38a] Since hemoglobin, hemin and hemochromogen derivatives may be converted respectively to spectroscopically practically identical cyan-methemoglobin,[38a] hemin dicyanide,[38b] and hemochromogen monocyanides,[38b] the cyanide derivatives were used for the quantitation of total hemin pigments in the various samples.

The comparison of the absorption spectrum data upon the peritoneal fluid and gut contents with known hemoglobin derivatives was materially aided by reliable information upon the latter, available from extensive work in the laboratory of one of us (DLD).

CLINICAL COURSE

Six of the seven animals responded in similar manner to the procedure and died between 28.25 and 48 hours after operation, with an average survival

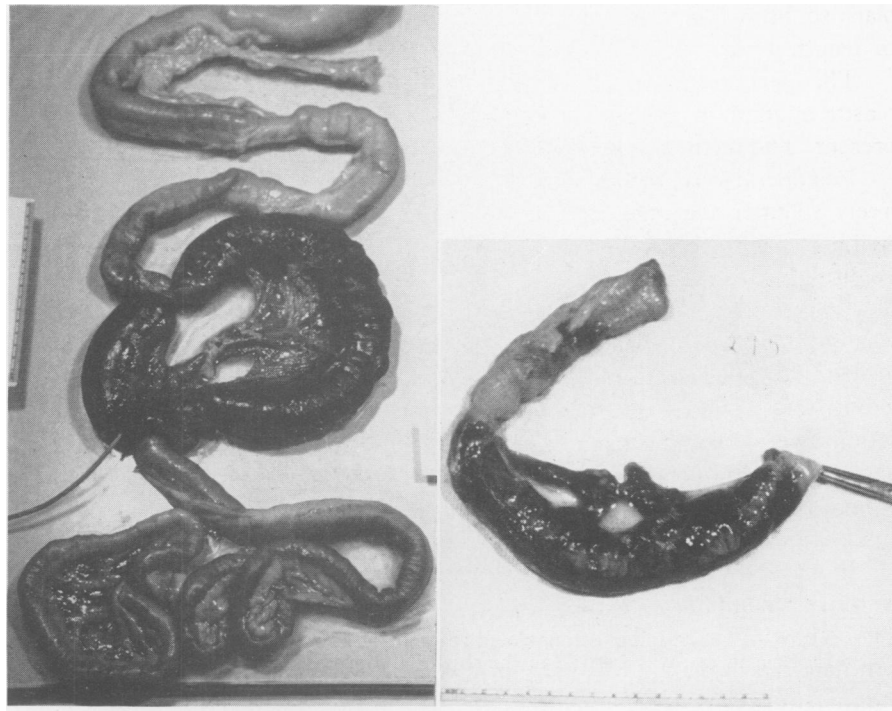


FIG. 2 FIG. 3

FIG. 2.—Photograph of the strangulated segment from dog. No. 365. This segment measured 75.0 cm. in length.

FIG. 3.—Photograph of the resected segment of bowel from dog No. 295. The strangulated segment measured only 25.0 cm. in length and was markedly thickened. The sharp line of demarcation is clearly shown.

time of 36 hours. This represents a definite prolongation of life, for in untreated animals with a similar length of strangulated gut death usually occurs between seven and 24 hours.[39-46] These dogs exhibited a black, necrotic, gangrenous, nonperforated, elongated, dilated[39, 40, 47-49] segment of gut. The loops were elongated some 25 to 50 per cent, and the wall was moderately to markedly thinned out (Fig. 1), but in no case had perforation occurred. There was an extremely sharp line of demarcation above and below the strangulated segment, and we found none of the changes in normal bowel described by Moon and Morgan.[41] One of these six animals (No. 365) demonstrated a

volvulus at autopsy, with a venous obstruction to the proximal obstructed bowel distal to the segment which had been purposely strangulated. The strangulated segment in this animal measured 75.0 cm. in length (Fig. 2). As there was no evidence of leakage at the proximal turned-in end nor at the entrance of the tube into the gut, this animal is included in the series and merely represents a more extensive strangulation.

The seventh animal (No. 295) lived for 75 hours, at which time resection of the strangulated segment was performed. The resected segment was blackish brown in color, extremely thickened, and measured only 25.0 cm. in length (Fig. 3).

The peritoneum in all cases revealed mild inflammatory changes and plastic exudate in the region of the loop, but in no case were necrotic areas present. The picture was never that of a bacterial peritonitis.

Postoperatively, the animals remained in relatively good condition, moving freely about in the cage up until one to four hours of death. At this time a striking change occurred. The animals obviously became sicker. Retching and vomiting, which had begun in all cases between eight and 14 hours, consisting of a foul smelling bloody fluid, became severe and constant. This final period was quite similar to that observed by Blain *et al.*[47] and Blain and Kennedy[48] in their dogs. Death occurred very suddenly and was preceded by convulsive movements of the extremities and gasping respirations. Femoral arterial pulsations were easily palpable in all cases up until several minutes of death, and the animal did not appear to be in clinical shock. Five of the six animals which died developed a terminal rise in the temperature to 103 to 107.6° F. just before death, and three of these were over 105° F.

It may be noted in Table II that the hematocrit and hemoglobin values were well maintained throughout the course of survival, only one animal (No. 347) showing a moderate fall. Large amounts of fluids were required to maintain the animals. The total fluid intake ranged between 3000 and 6700 cc. Administration of whole blood varied from 15.0 to 72.0 cc. per Kg. per 24 hours and of 5 per cent glucose in saline from 100 to 340 cc. per Kg. per 24 hours. The amount of peritoneal fluid removed over the course of survival varied from 603 to 1573 cc.

A study of the gut contents and peritoneal fluid revealed a constant sequence of events which was borne out by detailed chemical, bacteriologic, and spectrophotometric studies.

Within two to four hours after operation a small amount of reddish-black, odorless, coagulable fluid with a specific gravity between 1030 and 1040 and a hemoglobin content similar to that in the blood was aspirated from the strangulated gut lumen. The amount of this fluid entering the lumen was small at first but increased as the damage to the gut wall increased. At around 12 hours this fluid became black in color, noncoagulable, had a foul odor, and the specific gravity fell to between 1015 and 1024. From this point on the gross character of the fluid did not change, but the volume markedly increased. This later fluid in the gut lumen has been similarly described in strangulated

closed loops,[39, 42, 43, 45, 50] in simple strangulation obstruction[47, 48] and in isolated jejunal loops.[51]

On the other hand, the peritoneal fluid at two to four hours was pink or strawberry colored, clear, odorless, and had a specific gravity between 1019 and 1027. The physical properties as well as the chemical studies (Table III, Fig. 4) revealed that this fluid owed its character to the presence of blood and unchanged hemoglobin and, as shown by Laufman and Method,[52] apparently was derived early almost entirely from the serosal side of the strangulated gut. This continued to be the type of fluid recovered from the peritoneal

TABLE II.—*Intake and output data, hemoglobin and Hematocrit Readings on the Strangulated Animals*

	Length of Survival in	Fluid Change First Noted	Intake					
			Blood		Glucose Saline		Gelatin	
Dog	Hours	(Hour)	cc./L of S	cc./Kg./24h	cc./L of S	cc./Kg./24h	cc./L of S	cc./Kg./24h
331	42	36	1085	65	5525	340	100	6
237	48	48	660	24	2800	101	340	12
235	32	28	980	72	2425	182	200	15
357	35½	34	695	31	2275	101	100	5
347	30	29	805	38	2200	104	400	19
295	75*	..	550	15	4500	120	200	5
365	28¼	28	1000	50	2455	125	330	17

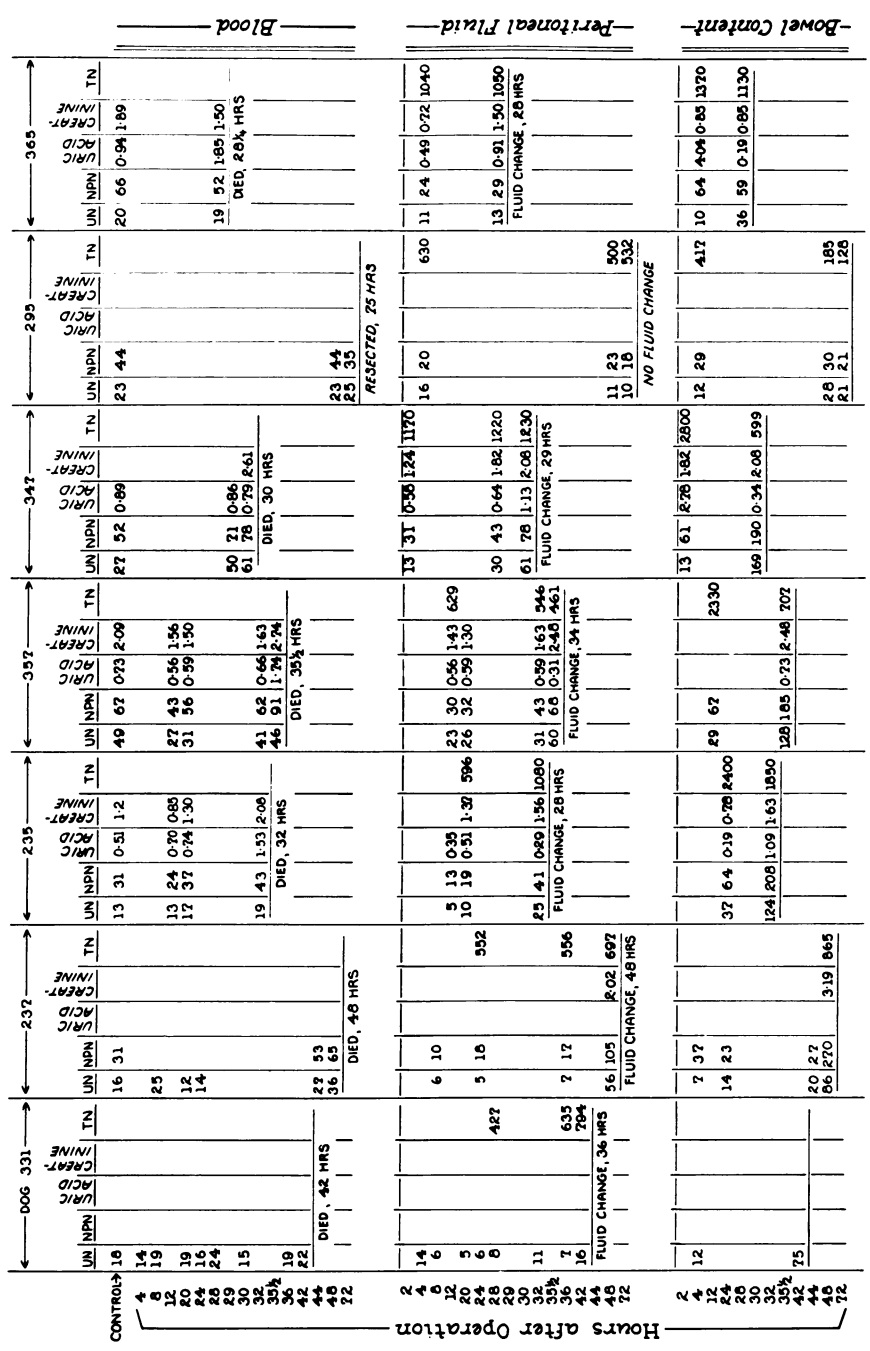
	Output									
	Peritoneal Fluid		Gut Contents		Urine and Vomitus		Hematocrit		Hemoglobin	
	cc./L of S	cc./Kg./24h	cc./L of S	cc./Kg./24h	cc./L of S	cc./Kg./24h	Initial	Terminal	Initial	Terminal
	1080	65	87	5	4040	245	55	57	20	19
	603	22	53	2	2450	89	47	54	16	18
	1400	106	38	3	1495	113	41	46	14	16
	1098	48	47	2	1290	58	39	40	13	14
	845	41	535	26	615	29	56	37	19	13
	674	18	115	3	2425	65	45	43	15	15
	1573	80	247	12	1380	70	52	49	18	16

* This animal never developed the fluid change, and the strangulated segment was resected at 75 hours.

cavity for a relatively long period of time. During the early stages this fluid was very abundant but decreased as the process progressed, possibly due to a thrombosis of the serosal vessels[52] or of the mesenteric veins proximal to the ligature.[22, 49] At variable stages, corresponding closely with the abrupt change in the clinical condition of the animal, the fluid recovered from the peritoneal cavity changed to a reddish black and later to a black fluid very similar in its physical and chemical characteristics to the bowel contents (Table III) (Fig. 4). The death of the animal occurred within one to four hours after the appearance of this fluid in the peritoneal cavity. The animal, which lived for 75 hours and was then reoperated upon, never developed the black fluid either in the gut or in the peritoneal cavity. Undoubtedly some degree of

TABLE III.—*Studies on the Nitrogenous Substances in the Blood, Peritoneal Fluid and Gut Contents*

(All values in mg/100 cc.)



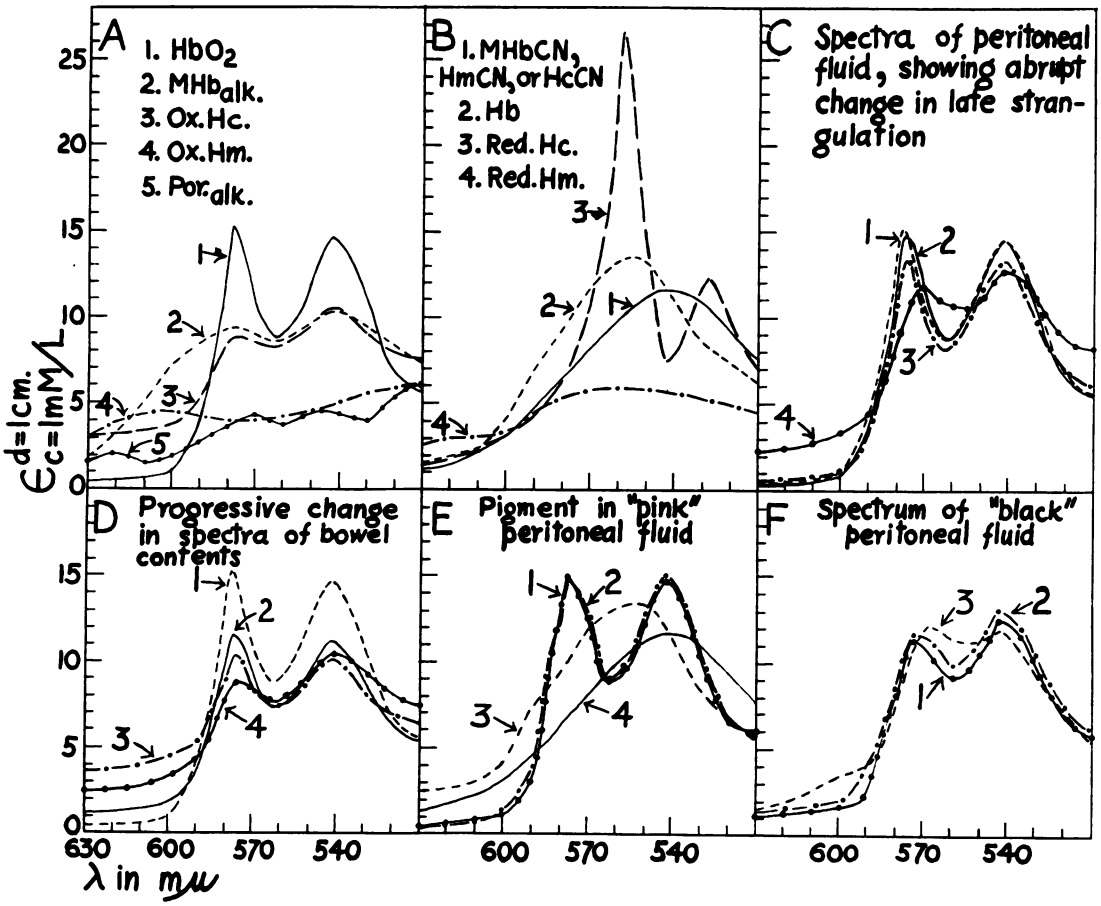


FIG. 4

FIG. 4.—Character and identification of absorption spectrum curves obtained from peritoneal fluid formed after the experimental intestinal strangulation (C, E, and F) and from the contents of the strangulated bowel segment (D). Absorption spectrum curves obtained from blood or derived from the hemoglobin of blood are presented for comparison (A and B).

A.—Curve 1, HbO_2, oxyhemoglobin;[59] Curve 2, $MHb_{alk.}$, alkaline methemoglobin, pH 9.15;[60] Curve 3, Ox. Hc., oxidized globin hemochromogen or globanferriprotoporphyrin;[61] Curve 4, Ox. Hm., oxidized hemin or ferrihemin;[61] Curve 5, $Por_{alk.}$, alkaline porphyrin.

B.—Curve 1, MHbCN, cyanmethemoglobin;[59] HmCN, hemin diacyanide;[62] or HcCN, monocyande derivative of oxidized globan ferriprotoporphyrin cyanide,[62, 63] derived respectively from 1 or 2 in A, 4 in A, and 3 in A; Curve 2, Hb, reduced or deoxygenated hemoglobin, derived from 1 or 2 in A by addition of hydrosulfite, $Na_2S_2O_4$; Curve 3, Red Hc. (reduced globin hemochromogen or globan ferroprotoporphyrin[61, 63] derived from 3 in A by addition of $Na_2S_2O_4$; Curve 4, Red. Hm. (reduced hemin or ferrohemin,[61] derived from 4 in A by addition of $Na_2S_2O_4$).

C.—Absorption spectrum curves of peritoneal fluid (from dog No. 357) removed at different times following establishment of strangulation obstruction. The curves illustrate the abrupt appearance (reflected in the abrupt change in color from "pink" to black) of the abnormal spectrum, Curve 4. Curve 1, unchanged oxyhemoglobin (same as 1 in A); Curve 2, at 4 hours, original total pigment concentration as MHbCN equals 0.649 Gm. per 100 ml.; Curve 3, at 32 hours, original total pigment concentration as MHbCN equals 0.387 Gm. per 100 ml; Curve 4, at 35 hours, original total pigment concentration as MHbCN equals 1.14 Gm. per 100 ml. (Legend continued on opposite page.)

revascularization occurred in the strangulated loop of this animal. Microscopically, the mucosal layer was intact whereas in the animals which died varying degrees of destruction were present.

CHEMISTRY

Blood. No significant change was noted in the chlorides, calcium[47, 48] or potassium.[53] The CO_2 combining power was moderately decreased.[47, 48] The amylase in the blood was decreased markedly within 12 to 24 hours following anesthesia and operation.[54] Eight hours after strangulation the serum lipase was 1.0 cc. or above in three of the six animals in which studies were made, and in one of the three it was also elevated at death. We have attached much accuracy to our determinations of serum lipase in the dog[55] and feel these elevations to be significant.

Peritoneal fluid. The protein content of the peritoneal fluid was in most instances between 3.4 and 4.5 Gm. per 100 cc.[45] The hematocrit of the early peritoneal fluid usually ranged from one up to less than six although in one animal (No. 347) values of 14 to 28 were obtained. No hematocrit readings could be obtained in the reddish black or black peritoneal fluid. The chloride content of the peritoneal fluid was slightly higher than that of the blood, and in two animals peritoneal fluid potassium levels were not elevated.[53] The amylase in the early peritoneal fluid varied directly with that of the blood.

Nitrogen studies in blood, peritoneal fluid and gut contents. We attach no significance to slight variations in the uric acid and creatinine which we obtained (Table III), and in no case did we find values for creatinine as high as those reported by Cooke, Rodenbaugh and Whipple.[56] In all the dogs which died, except the animal with the 75.0 cm. strangulation (No. 365), there was a slight to moderate increase in the blood urea nitrogen[39] and blood nonprotein nitrogen.[39, 45, 47, 48] The increase averaged 65 per cent for the blood urea nitrogen and 55 per cent for the nonprotein nitrogen. In the peritoneal fluid

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D.—Absorption spectrum curves of contents of strangulated bowel segment (from dog No. 357), showing progressive change at an appreciably earlier time than in the peritoneal fluid (curves in C) toward fluid with the characteristic abnormal spectrum. Curve 1, unchanged oxyhemoglobin (same as 1 in A); curve 2, at 12 hours, original concentration of total pigment as MHbCN equals 9.81 Gm. per 100 ml.; Curve 3, at 27 hours, original concentration of total pigment as MHbCN equals 2.12 Gm. per 100 ml.; Curve 4, at 35 hours, original total pigment concentration as MHbCN equals 2.14 Gm. per 100 ml.

E.—Identification of spectrum of "pink" peritoneal fluid (from dog No. 235) as that of unchanged oxyhemoglobin. Curve 1, at 24 hours, original concentration of total pigments as MHbCN equals 0.432 Gm. per 100 ml., pH equals 8.0 (compare with curve 1 in A); Curve 2, obtained after addition of solid cyanide to solution yielding Curve 1 (no change); Curve 3, obtained after addition of solid $Na_2S_2O_4$ to solution yielding Curve 1 (compare with Curve 2 in B); Curve 4, obtained after addition of ferricyanide (for oxidation) and cyanide to solution yielding Curve 1 (compare with Curve 1 in B). Practically the same curve as 1 was obtained from a specimen removed at 28 hours.

F.—Abnormal behavior of pigment in "black" peritoneal fluid (from dog No. 235) towards addition of cyanide or $Na_2S_2O_4$. Curve 1, at 32 hours, original concentration of total pigment as MHbCN equals 4.46 Gm. per 100 ml., pH equals 9.2 (compare with Curve 4 in C and D); Curve 2, obtained after addition of solid cyanide to solution yielding Curve 1 (see the text); Curve 3, obtained after addition of solid $Na_2S_2O_4$ to solution yielding Curve 1 (see the text).

of the same group of animals the urea nitrogen showed an average increase of 362 per cent and the nonprotein nitrogen of 353 per cent. It will also be noted that this increase was not a gradual one but occurred suddenly during the late stages after the black fluid had appeared. The urea nitrogen and nonprotein nitrogen of the gut contents showed an average increase of 704 per cent and 309 per cent respectively. Here, also, it would seem that a late increase occurred (No. 237).

TABLE IV.—*Bacteriologic Studies on the Blood, Peritoneal Fluid and Gut Contents*

Dog No.	Peritoneal Fluid		Blood	Gut Contents
	Pink	Black or Red Black		
331	Hemo. clostridia B. coli Strep. viridans	Hemo. clostridia B. coli Non-hemo. strep.	Negative throughout	
237	Hemo. clostridia B. coli Salmonella Non-hemo. strep.	Hemo. clostridia B. coli Salmonella Non-hemo. clost. Non-hemo. strep.	36 h.—negative 48 h.—B. coli Non-hemo. clost.	
235	Hemo clostridia B. coli Hemo. strep. Non-hemo. strep.	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost.	Negative throughout	
357	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost. A. aerogenes	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost. A. aerogenes B. proteus	32 h.—Negative 34 h.—A. aerogenes 35 h.—Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. A. Aerogenes B. proteus	Hemo. clostridia B. coil Hemo. strep. Non-hemo. strep. Non-hemo. clost. A. aerogenes B. proteus
347	Hemo. clostridia B. coli Non-hemo. strep. Non-hemo. clost. A. aerogenes	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost. B. proteus	Negative throughout	Hemo. clostridia B. coli Non-hemo. strep. Non-hemo. clost. B. proteus
295	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost. Eberthella		Negative throughout	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost. Eberthella
365	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. A. aerogenes	Hemo. clostridia B. coli Hemo. strep. A. aerogenes	Negative throughout	Hemo. clostridia B. coli Hemo. strep. Non-hemo. strep. Non-hemo. clost. A. aerogenes

Bacteriology. The peritoneal fluid has been found to be sterile at four to six hours[43, 57] and even as late as 19 to 20 hours.[47-49] In general, we found the peritoneal fluid to be sterile up until 14 to 20 hours, at which time the flora of the strangulated gut began to appear, and the late pink peritoneal fluid contained, qualitatively at least, almost identically the same organisms as found

in the red-black or black peritoneal fluid (Table IV). In three of the animals in which the gut contents were cultured just prior to death, the black fluid contained the same organisms as were found in the gut. It will be noted, however, that in these cases the same organisms were present in the pink fluid as early as 20 hours. In the animal which was resected at 75 hours the peritoneal fluid contained qualitatively the same organisms at 29 hours as were recovered from the resected segment at 75 hours. Hemolytic clostridia, *B. coli,* and nonhemolytic streptococcus were present in the peritoneal fluid in all cases.[58]

Positive blood cultures were obtained just before death in two animals. In both cases the black fluid was present in the peritoneal cavity at the time positive cultures were obtained.

Spectrophotometric findings. In Figure 4, A to F and its accompanying legend, typical results of the spectrophotometric measurements on the peritoneal fluid and bowel contents are presented together with an interpretation of the significance of the spectra. The latter is aided by a comparison with absorption spectrum curves obtained from normal hemolyzed blood or derived from the hemoglobin in blood by physical or chemical treatment (A and B, Fig. 4). The following points appear to be established unequivocally:

1. The absorption spectrum of samples of the pink or strawberry colored peritoneal fluid, withdrawn sometimes as late as 32 hours after strangulation, was essentially that of unaltered oxyhemoglobin (E, Fig. 4).

2. The absorption spectrum of the black peritoneal fluid was markedly and characteristically different from that of oxyhemoglobin and quite identical with the abnormal spectrum of the contents of the strangulated bowel segment. Detailed spectrophotometric evidence cannot be presented here, but the findings (in other experiments than those reported in Figure 4) lend themselves to the clear interpretation that the degree of alteration of the spectrum of peritoneal fluid from the character of Curve 2 towards Curve 4 in C depends on the proportion of two components in the mixture, namely, the relative amounts of pink peritoneal fluid and black bowel contents.

3. In contrast with the abrupt late change in spectroscopic character found in the peritoneal fluid, the alteration towards the abnormal spectrum in the bowel contents was early and progressive (D, Fig. 4).

4. It may be seen that the abnormal spectra of the bowel contents or of the late peritoneal fluid bear a superficial resemblance to either alkaline methemoglobin (Curve 2 in A), or still more closely to oxidized globin hemochromogen (Curve 3 in A). Both methemoglobin and oxidized hemochromogens should react with cyanide to yield the spectrum typified by cyanmethemoglobin (Curve 1 in B). An examination of the curves in F makes it clear that the abnormal spectrum of the black peritoneal fluid cannot be accounted for by the presence of appreciable amounts of methemoglobin or oxidized hemochromogens, for there was unexpectedly little change after the addition of cyanide (2F). After the addition of $Na_2S_2O_4$ (3F) if methemoglobin were present, a change toward 2B should have been found, or if typical hemo-

chromogens were present in appreciable amounts, a change toward the striking spectrum 3B should have been found.

The atypical behavior of the black peritoneal fluid towards cyanide and $Na_2S_2O_4$ suggests that we are dealing with an unusual pigment or pigments. It should be mentioned that most of the pigment in the black bowel contents and black peritoneal fluid were hemoglobin or hemin derivatives since they responded typically to the addition of ferricyanide plus cyanide.

5. To conserve space the spectrophotometric studies upon the blood have not been presented. These demonstrate unequivocally that the abnormal pigment appears in the blood but only very soon after or simultaneously with its appearance in the peritoneal fluid.

DISCUSSION

That shock through the local loss of fluid[45] may account for death in experimental long loop strangulations is amply demonstrated.[40, 42, 45, 46, 57, 64, 65] However, even with adequate treatment for shock, life is prolonged but little.[22, 47, 48] That penicillin when combined with treatment for shock, dehydration, and electrolyte imbalance may prolong life in strangulation obstruction has been shown also and would indicate that bacteria or their products probably play a role in the cause of death.[47, 48] Here again the protection afforded is limited, and the existence of some other lethal agent is further indicated by the series herein reported.

The lethal action of the contents of a strangulated loop of gut has been shown by many workers,[40, 42, 43, 50, 66, 67] but heretofore there has been no conclusive evidence for the absorption into the blood stream of the intraluminal contents, nor can it be stated that death would result even if such substances were absorbed.

The occlusion of the veins to a segment of bowel, as occurs in experimentally produced strangulation, precludes this route as a source of absorption. Lymphatic absorption has been incriminated by some investigators,[40, 43, 49] but others have failed to prolong life by obstructing the lymphatics.[67, 68] The likeliest source of absorption would appear to be from the peritoneal cavity.[44, 45, 68] However, in practically all instances reported, the peritoneal fluid removed from strangulated animals has proved to be nontoxic when injected into other animals,[42-46, 50, 57, 69] thus indicating that noxious agents from the lumen had not entered the peritoneal fluid, or else that the noxious agents were not present in sufficient amount to be lethal when injected into other animals.[67]

Our studies have revealed that late in the course of strangulation obstruction in animals intensively treated to avoid hemorrhage, shock, dehydration, and electrolyte imbalance, the bowel wall becomes permeable to its intraluminal contents, and this fluid then passes out into the peritoneal cavity and thence into the blood stream. We believe, as do others,[39, 40, 45, 49, 56, 64] that the pink peritoneal fluid is but a filtrate of the circulating blood. We also think that the development of the reddish-black or black fluid is due to a filtration of

the strangulated gut contents through the devitalized bowel wall into the peritoneal cavity. Even after the complete occlusion of the venous channels, evidence of permeability of the gut wall to its intraluminal fluid occurred in none of our animals before 28 hours. This is longer than the length of survival of animals in which shock, dehydration and electrolyte balance have not been combatted.

That this black fluid is a "diluted" counterpart of the gut contents is also shown and would be expected in view of the continued outpouring of the pink or plasmalike fluid from the peritoneal surfaces in the presence of a devitalized segment of intestine within the peritoneal cavity.[57]

The death of the animal followed shortly after the development of the reddish-black or black fluid in the peritoneal cavity. In view of this fact and the known marked toxicity of the lumen contents, it would appear that some lethal factor was present in this later fluid. It is unlikely that the living bacteria or their end products are directly concerned with the death of the animal.[43, 57] While it is true that the black fluid contained, qualitatively, the same organisms as did the lumen contents just before death, it must also be remembered that these same organisms were present in the pink fluid from around 16 to 20 hours onward, yet death did not occur until a short time after the development of the black peritoneal fluid. The important role of the organisms indirectly by their action on the devitalized mucosa, however, has been indicated by Sarnoff and Fine[22] and Blain, *et al.*,[47, 48] and it is likely that the prolongation of life in the penicillin treated group of animals reported by Blain *et al.*[47, 48] was due to the fact that the destructive action of the organisms on the bowel wall was delayed, thereby lengthening the time in which the gut became permeable to its intraluminal contents.

If it is true that a noxious agent formed in the gut and absorbed into the blood stream is the cause of death in these animals, then much clarification of the route of absorption is afforded by our studies. Although the characteristic luminal contents were present within the lumen as early as 12 hours, death did not occur until soon after the reddish-black or black fluid had appeared in the peritoneal cavity, and in no case were we able to demonstrate spectrophotometrically the hemin or hemoglobin derivative in the blood stream until after it had appeared in the peritoneal cavity. The absorption from the lymphatics of the strangulated gut would, therefore, appear to be negligible.

While the characteristic absorption spectrum curve typifying black bowel contents and black peritoneal fluid has been defined, the identity of the pigment or pigments responsible for the abnormal spectrum has not been established. It remains for future investigation to establish whether the curve represents hemoglobin derivatives not hitherto described and originating from the blood pigment under the abnormal conditions in the strangulated bowel segment, or whether the spectrum is that of a mixture of common hemoglobin derivatives with less usual ones. Among the latter may be mentioned sulfhemoglobin[59] and porphyrins,[70] both of which types of pigments could conceivably

be formed in the intestine from hemoglobin. At present we have no evidence that either of such pigments is involved.

It is important to state clearly that at this stage we have no evidence whatever directly implicating the abnormal pigment or pigments with responsibility for the toxicity. Such close hemoglobin derivatives as methemoglobin are essentially nontoxic,[71] and at present there is little evidence that other derivatives or relatives of hemoglobin may be toxic, with the possible exception of porphyrins. It is sufficient to state that the pigments responsible for the abnormal spectrum are contained in the black peritoneal fluid, characterize it, and give evidence for its intestinal origin.

SUMMARY AND CONCLUSIONS

1. Late in the course of strangulation obstruction the bowel wall becomes permeable to its intraluminal contents, and this characteristically colored fluid passes out into the peritoneal cavity and is then absorbed into the blood stream. The death of the animal occurs soon after the appearance of this late black or reddish-black fluid in the peritoneal cavity.

2. By spectrophotometric analysis we have demonstrated that the character of the intraluminal contents is due in part to the presence of a hemin or hemoglobin derivative hitherto unreported *in vivo,* and by this method we have directly followed its passage from the gut lumen into the peritoneal cavity and from thence into the blood stream.

3. In view of the close correlation between the appearance of the black peritoneal fluid and the demise of the animal, it would appear likely that a lethal agent was present in this late fluid. If this is the true explanation, the "toxicity" of this fluid should be demonstrable on injection into recipient animals, and the subsequent report is concerned with this phase of the problem.

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